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Before the
FEDERAL COMMUNICATIONS COMMISSION
Washington, D.C. 20554

In the Matter of	)	
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Guidelines for Evaluating the Environmental Effects of Radiofrequency Radiation	)))	ET Docket No. 93-62

TO: The Commission

COMMENTS OF
MEMBERS OF THE ARRL BIO-EFFECTS COMMITTEE

These comments are offered in response to the Commission's Notice of Proposed Rule Making in the above captioned matter by members of the Committee on the Biological Effects of Radio Frequency Energy of the American Radio Relay League, speaking as individuals and not as representatives of the League. We are amateur radio licensees who have been appointed by the ARRL Board of Directors to provide advice to the Board concerning the possible health considerations involved in various amateur radio activities. Several of our members are actively engaged in medical research in this field.

AMATEUR RADIO LICENSEES AND EMR HAZARDS

We believe that this proceeding poses a difficult dilemma for the Commission in regulating the amateur radio service. Traditionally, amateur radio operators have been categorically exempt from the environmental review required of many other FCC-

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licensed services. Amateurs have not been required to determine the electromagnetic field intensities associated with their operations, either by calculations or measurements. Nor have amateurs been required to certify to the Commission that their activities pose no health hazard to the operators themselves, or to their families and neighbors.

Clearly, this policy has been appropriate in most respects. The Commission's own field measurements of electromagnetic fields near amateur radio stations, conducted in 1990, revealed that few amateur activities produced fields in excess of the ANSI C95.1-1992 guideline, which the Commission now proposes to adopt as a processing guideline for its licensees. The very nature of most amateur radio activities precludes exposure to fields exceeding the ANSI guideline. Most amateurs use low or moderate power levels and operate their equipment only intermittently on an avocational basis. And most amateurs who do utilize transmitter power approaching the maximum set by the Commission's rules also utilize directional antennas mounted 40 to 100 feet above ground level on a tower. The Commission's measurements indicated that such installations produce only minimal energy levels in inhabited areas.

At the same time, thousands of amateurs engage in public service communications, setting up temporary stations near scenes of natural disasters such as hurricanes, floods, firestorms and earthquakes. These amateur activities would be severely inhibited if a formal environmental review were required before a mobile, portable or other temporary station could be activated. Most amateurs simply do not possess the requisite equipment, technical skills and financial resources to comply with the Commission's normal environmental review requirements.

However, certain amateur radio activities do produce significant field intensities in populated areas. A 100-watt vehicular mobile installation operating in the VHF range (e.g., the popular 144 MHz amateur band) may well produce fields in excess of the C95.1-1992 guideline inside the vehicle. Hand-held transceivers--which are very widely used by radio amateurs--may produce significant localized fields near the antenna. Also, some amateurs employ indoor antennas in the face of zoning regulations or restrictive covenants that preclude the use of high, outdoor antennas.

Moreover, a small number of amateurs utilize a combination of high power and very high gain antennas for specialized forms of VHF-UHF amateur activity such as earth-moon-earth ("moonbounce") communication. E.m.e. stations typically utilize antennas with 20 to 30 dB. of forward gain over a dipole in combination with the maximum transmitter power permitted by the Commission's rules. Fortunately, the amateur licensees who engage in such sophisticated activities tend to be both experienced and technically competent. Although e.m.e. stations are sometimes located in residential neighborhoods--and their highly directional antennas are occasionally pointed at the horizon to take advantage of the enhanced performance resulting from ground gain--most e.m.e. operators are careful not to point their arrays toward inhabited places.

Moonbounce communication is a growing specialty within amateur radio. During the two weekends of the 1993 ARRL E.M.E. Contest, one station in eastern Canada utilized a 150-foot parabolic dish antenna--an antenna normally reserved for scientific research--and completed two-way moonbounce contacts with more than 550 other amateur stations. During the same two-weekend period, several other stations that employed only amateur-owned multi-bay Yagi antennas completed moonbounce contacts with more than 250 stations each.

It seems clear that most amateurs cannot be expected to perform the kind of environmental review required of many other Commission licensees. But it is also clear that some amateur licensees engage in operating activities that generate significant electromagnetic fields.

We would suggest that the Commission refrain from subjecting all amateurs to the burdensome requirements of environmental processing, not only because it would be prohibitively expensive for many amateur licensees but also because it would inundate the

Commission's staff with paperwork if such requirements were adopted for a service with 625,000 licensees.

Instead, we would urge the Commission to take the lead in educating all amateurs to the need for prudent operating practices. The Commission could prepare and promulgate, in Part 97 of its rules, a tabular chart showing the calculated field intensities at various distances from antennas having various directive patterns, driven by transmitters of various power output levels. The chart might indicate the thresholds set by the 1992 ANSI guideline, should the Commission choose to adopt it as a standard.

Also, there are other steps the Commission could take to increase amateur awareness of safe operating practices. A few practical questions about electromagnetic radiation safety could be included in each amateur licensing examination, for example. Finally, each applicant for an amateur license could be required to certify on Form 610, the basic licensing form, that he/she has read the FCC guidelines, understands them, and agrees to comply.

We believe simple, cost-effective measures such as these would be a major step toward increasing amateur awareness of safe practices. Given sufficient information about the potential hazards of utilizing high power in a vehicular mobile installation (or with an indoor antenna), for example, we believe most amateurs would adopt the philosophy of prudent avoidance as developed by Professor M. Granger Morgan at Carnegie Mellon University.

As conceived by Dr. Morgan, prudent avoidance obligates the user of electromagnetic devices to avoid unnecessary exposure in the home and the workplace as a common-sense response to potential--but not yet proven--health hazards. Already, the r.f. safety sections of major ARRL publications urge radio amateurs to practice prudent avoidance wherever possible.

We believe the Commission could play a very positive role in this educational process by encouraging amateurs to think about the full range of possible consequences of their activities, and to act responsibly in dealing with safety issues.

INADEQUACIES OF THE 1992 ANSI GUIDELINE

In the instant Notice, the Commission inquired about the adequacy of ANSI C95.1-1992 for use as a processing guideline. We wish to state, in the strongest possible terms, that the ANSI guideline fails to consider two crucial issues in the assessment of electromagnetic radiation safety: the effect of low-frequency modulation, pulsing and keying of radio frequency signals, and the growing body of evidence that athermal affects of electromagnetic energy must be taken into account.

We are attaching to these Comments, at Appendix A, a paper entitled "Mechanisms Mediating Athermal Bioeffects of Nonionizing

Electromagnetic Fields," presented by W. Ross Adey, M.D., at the International Union of Radio Sciences German National Assembly in Kleinheubach on October 7, 1993. It cites numerous recent studies documenting athermal affects of electromagnetic energy on living organisms--at intensities below the ANSI C95.1-1992 guideline. When the current laboratory research is combined with the mounting epidemiological evidence of an association between electromagnetic field exposure and certain cancers, this issue must not be ignored. There cannot now be any doubt that very low level fields have demonstrable biological effects, particularly when a radio signal is modulated, keyed or pulsed at certain low frequencies.

Unfortunately, the ANSI C95.1-1992 guideline may become a de facto standard for both occupational and non-occupational exposure. In developing C95.1-1992, Subcommittee 28 of the IEEE Standards Coordinating Committee chose to ignore the significant volume of highly credible scientific evidence on athermal effects. Even worse, the ANSI/IEEE guidelines appear to have become a refuge for special interests for whom the very existence of health problems at athermal levels of exposure would have important (and costly) consequences.

In its Notice in this proceeding, the Commission alluded to some of the questions that have been raised concerning the adequacy of C95.1-1992. We agree that the guideline adopted by the

National Council for Radiation Protection and Measurement addresses important issues that were ignored by IEEE Subcommittee 28. We would also point out that both public and private sector organizations are now adopting occupational exposure standards that are far more stringent than C95.1-1992 is even for non-occupational exposure. For example, both the Applied Physics Laboratory at Johns Hopkins University and the Advanced Weapons and Survivability Directorate at Phillips Laboratory, Kirtland Air Force Base, have adopted exposure limits of .1 mw/cm^2 for the entire frequency range from 30 MHz to 100 GHz.

Given all of these factors, we believe that if C95.1-1992 is to be adopted by the Commission at all, its standard for uncontrolled environments is the least stringent standard that the Commission ought to consider using in its environmental review of licensees. In fact, the Commission would be on firmer scientific ground if it added to this guideline a consideration of the effects of keying, pulsing or low-frequency modulation on the r.f. signals radiated by its licensees.

CONCLUSION

Radio amateurs have a proud history of voluntary compliance with the Commission's rules. While it is clear that many amateurs have little knowledge of r.f. radiation hazards (let alone an accurate means of measuring the fields associated with their stations), the FCC could greatly increase amateur compliance with ANSI C95.1-1992--or whatever standard the Commission may ultimately adopt--by including a clear tabular chart in Part 97 detailing those amateur activities most likely to result in excessive exposures. While amateurs should be informed about good r.f. safety procedures (and required to practice them), the Commission's traditional environmental processing system would seem impractical for the amateur service. On the other hand, if amateurs are given clear guidelines to follow in their operating practices and the placement of their antennas, we believe most will make a good faith effort to comply.

Respectfully submitted,

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January 7, 1994

APPENDIX A

Mechanisms Mediating Athermal Bioeffects of Nonionizing Electromagnetic Fields

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Presented at the
International Union of Radio Sciences
German National Assembly, Kleinheubach
October 7, 1993

Abstract

Effective radiated power levels from most hand-held RF devices, such as mobile telephones, have been progressively reduced to 1 watt or less. Even when operated in close proximity to the human body, fields from these devices are too weak to produce biologically significant heating. Their biological effects are therefore described as ***athermal*** responses. They occur in ELF fields, and in RF/microwave fields that are pulse- or amplitude-modulated at ELF frequencies. Biological transduction and signal amplification are increasingly understood as a structural and functional hierarchy, beginning at the ionic and ***free radical*** level, and extending progressively through biomolecular sequences to cellular and tissue levels; and finally to major biological systems and to the whole organism. It is generally agreed that first detection of ELF and ELF-modulated RF/microwave fields occurs at membranes that enclose all cells. Magnetic field bioeffects involving free radicals may extend down to zero field energy; energy of thermal collisions (kT) does not set a threshold. Epidemiological studies describe immune deficiencies, altered growth and development, and cancer. Tumor types most frequently reported are leukemia, lymphoma, malignant brain tumors (gliomas) and male breast cancer. Syntheses and models now bridge between epidemiology and laboratory research in modeling these enhanced tumor risks. When cell-cell communication is disrupted by chemical cancer promoters, unregulated cell growth may occur. This action at cell membranes is enhanced by imposed fields, which may thus act jointly with chemical agents as ***copromoters*** in tumor formation. Revision of safety standards for ELF/RF exposure must await further studies in basic biological mechanisms, rather than an epidemiological approach.

1. Introduction

Civilized societies expose the human organism to a broad spectrum of man-made environmental electromagnetic fields from conception to death. These exposures now cover the spectrum from ELF to millimeter waves. There is now consistent evidence from a wide range of laboratory studies that their biological actions do not relate to tissue heating.

In the case of hand-held RF devices, such as mobile telephones, radiated powers below 1 watt are generally too weak to produce biologically significant heating, even when operated close to the body. Nevertheless, these and much weaker ELF and RF fields can elicit major biochemical responses in healthy and diseased body cells.

Moreover, in many of these ***athermal*** biological responses, there is a specificity relating to physical parameters of the imposed field. The responses are often "windowed" with respect to narrow bands of ELF frequencies, or of ELF modulation frequencies; or "windowed' with respect to field incident energy; or to onset or termination of an exposure epoch. These constraints argue strongly against the ***equilibrium*** thermodynamics of heating as a basis for interaction. On the other hand, much of the available evidence meets criteria for ***nonequilibrium*** electrodynamic systems, associated with highly cooperative processes in populations of elements behaving coherently at a submolecular level.

2. The Question of Possible Health Hazards Related to Environmental Electromagnetic Field Exposure

Epidemiological studies have examined domestic and industrial exposures to both ELF and RF/microwave fields. With progressive refinement in environmental field measurements, in personal dosimetry techniques, and in a growing awareness of possible joint actions of electromagnetic fields and chemical substances in the pathogenesis of human disease, there are now certain emergent avenues for concern. The primary focus of epidemiological studies has been cancer risk, with secondary emphasis on immune deficiencies (also cancer related) and disorders in pregnancy, growth and development.

2.a. Exposure to ELF Fields

Human exposure to ELF fields is primarily at 50 or 60 Hz in distribution and use of electric power in homes, in the environment, and in the workplace. Three benchmark domestic studies may be cited, since they have attempted a correlation with environmental field levels. They suggest an association of increased risk with long term exposure to ambient fields in excess of 0.2 uT.

Savitz et al. (1988) extended pioneering studies by Wertheimer and Leeper (1980) on childhood cancer and exposure to 60 Hz electric and magnetic fields. Using odds-ratio (OR) as an index of risk, raised risks were observed for total cancers (1.4), and larger ORs for leukemias (1.9), lymphomas (2.2), and soft tissue sarcomas (3.3). In relating risk to electric wiring configuration codes (as a surrogate measure of long-term magnetic field exposure), and by contrasting Very High and Low wiring code homes, they observed ORs of 1.5 for total cases, 2.0 for brain cancer, but 0.8 for lymphomas. Contrasts of Very High to Buried wire code homes produced larger but less precise ORs for total cases (2.3), leukemias (2.9), and lymphomas (3.3). Measured magnetic fields under conditions of low power use, with a cutoff score of 0.2 uT, showed a modest relation to cancer incidence (1.4).

In a case-control study of leukemia in children aged 1-10 years in Los Angeles County, London et al. (1991) related disease incidence to electric and magnetic fields in the home, using measurements, wiring configuration and self-reported appliance use. Their results support an association between childhood leukemia and wiring configuration (OR = 2.15), but not direct measurements of magnetic fields. Case incidence was higher amongst users of appliances producing high electric and magnetic fields (electric blankets, hair curling irons, black-and-white televisions and electric hair dryers).

Importantly, this study also evaluated leukemia risk of associated chemical factors. ORs were raised for incense use (2.78) and insecticide use inside the home (2.48). Parental occupational exposures were assessed during pregnancy, with strongest associations for mothers' exposure to nonionizing radiation (4.08) and fathers' exposure to spray paint (2.08). We shall consider further the joint actions of environmental electromagnetic fields and chemicals in tumor promotion, with fields as ***copromoters*** in the ***epigenetic*** model of carcinogenesis.

The first measured dose-dependence in cancer incidence from long term exposure to 50 Hz magnetic fields within 300 m of high voltage power lines comes from Swedish studies (Feychting and Ahlbom, 1992). Current loads were known on every kilometer of 15,000 km of 220 and 400 kV power lines between 1960 and 1985. Magnetic fields at varying distances from the line were calculated from annualized average current loads. For childhood leukemia, and with cut-off points at 0.1 and 0.2 uT, the relative risk (RR) increased to 2.7 for 0.2 uT and higher fields ($p = 0.02$). At an upper cut-off point of 0.3 uT, the RR was 3.8 ($p = 0.005$). In adults at field levels above 0.2 uT, RRs for both acute and chronic myeloid leukemia were 1.7. There was no increased risk for brain tumors in either children or adults.

Other ELF studies have pointed to joint actions of fields and chemical factors in malignant lymphoma in aluminum plant workers, with evidence of immuno-suppression (reversal of helper/suppressor blood lymphocyte ratios) in 14 of 23 workers (Davis and Milham, 1989); in male breast cancer in electrical workers in Norway (Tynes and Andersen, 1990) and the USA (Matanoski et al., 1990); in brain tumor (glioma) incidence in electricians (Preston-Martin et al., 1989; Loomis and Savitz, 1990); and in maternal (Savitz et al., 1990) and paternal (Johnson and Spitz, 1989) influences on brain tumor and leukemia incidence in the offspring. Increased risks of miscarriage are reported in American workers with video display terminals (Goldhaber et al., 1988), and in Finnish workers, this risk is dose-dependent in relation to VDT field levels (Lindbohm et al., 1992).

2.b. <u>Exposure to RF/Microwave Fields: Questions of Dose-Dependence</u>

In near-field exposures to RF/microwave fields, and in some far-field situations, absorbed energy may be sufficient to cause tissue heating. Individuals occupationally exposed to RF near-fields may be transiently exposed to thermalizing levels in environments otherwise predominantly athermal. Lacking the necessary field modeling and dosimetry, most epidemiological studies have not sought to quantify the separate contributions of thermal and athermal exposures to the total dose; nor have they considered concurrent exposures to power frequency magnetic fields.

A case-control study by the U.S. National Cancer Institute of brain tumor incidence in RF/microwave occupational exposures (Thomas et al., 1989) in the states of New Jersey, Pennsylvania and Louisiana concluded that all excess risk for primary brain tumors in white males aged over 30 years derived from jobs involving design, manufacture, installation or repair of electronic equipment (RR = 2.3). RRs were not increased in men exposed to RF/microwave fields but who never worked in electrical or electronics jobs. Risks of these malignant tumors (astrocytomas) increased to ten-fold for those employed 20 years or more. The authors emphasize concurrent chemical exposures to soldering fumes, solvents and a variety of chemicals as possible co-factors with RF/microwave fields in tumor promotion.

A small study of 10 Yugloslav microwave workers has examined blood lymphocytes for aberrant chromosome structure (Garaj-Vrhovac et al., 1990). Exposures ranged from 8 to 25 years (mean 15 years). Microwave power density at work sites ranged from 10 to 50 uW/cm^2, and was thus substantially below thermalizing levels. Blood lymphocyte cultures showed significantly increased numbers of micronuclei and chromosome damage after microwave exposure, but effects were less severe than in subjects exposed to vinyl chloride monomer. Since electromagnetic fields below the infrared lack photon energies to directly damage nuclear DNA by ionization, the investigators hypothesize that these effects may arise through metabolic paths involving free radicals.

3. Laboratory Research Related to Health Risks; Counterpart Studies

It is unfortunate that the elegantly intuitive epidemiological approach to medical disorders has become a relatively blunt tool in the search for mechanisms that mediate a myriad newly recognized human ills. Many of these are the unwitting result of new applications in high technology. There are special challenges in evaluating the role of a weak physical agent, such as nonionizing electromagnetic fields, where effective stimulus levels may be below thermal collisional energy in biomolecular substrates.

A search for the mechanistic basis of bioeffects of these athermal exposures requires a progressively finer focus on a biological hierarchy that descends from tissues to cells, to biomolecular organization, and finally to atomic substrates, specifically in free radicals, which may mediate physical events in first transduction of magnetic fields at the cellular level. Also, recent research emphasizes the likelihood that magnetic field bioeffects may involve a sequence of interactive mechanisms, rather than a single mechanism, consistent with the structural and functional hierarchy to be described.

3.a. Cell Membranes as the Site of Electromagnetic Field Transduction

Aggregates of cells form the tissues of higher animals. It is generally agreed that the first detection of ELF and ELF-modulated RF/microwave fields occurs on the membranes that enclose all cells. Cells are separated by narrow channels which are important in signaling from cell to cell, since they are windows on the electrochemical world surrounding each cell. Biomolecules, such as hormones, antibodies and neurotransmitters, move along them to reach binding sites on cell membrane receptors (Adey, 1992a).

These channels, typically not more than 150 A^0 wide, are also ***preferred pathways for intrinsic and environmental electromagnetic fields***, since they offer a much lower electrical impedance than cell membranes. Although this intercellular space (ICS) forms only 10 percent of the cross section of typical tissue, it carries at least 90 percent of any imposed or intrinsic current, ***directing it along cell membrane surfaces.***

Cell membranes are complex detectors, amplifiers, and couplers of weak surface electrical signals to the cell's interior. Cells also communicate with their neighbors by outward signals, faintly "whispering together" electrically and chemically, through signals that are also sensitive to electromagnetic fields (Adey, 1990a, 1992a).

Cell membrane ultrastructure is consistent with this sequence of signal detection and coupling from cell surface to interior. The essential structure of the cell membrane is a double layer of phospholipid molecules, about 40 A^0 thick, forming the ***plasma membrane***. A steady ***membrane potential*** of approximately 0.1 V exists across the plasma membrane, creating an enormous electric barrier of 10^5 V/cm, many orders of magnitude greater than weak components of environmental electromagnetic fields in fluid surrounding cells.

Numerous stranded protein molecules protrude through the plasma membrane from within the cell into the narrow "gutter" of the ICS. Tips of these strands are highly negatively charged and form a polyanionic surface sheet (the ***glycocalyx***). These tips form receptor sites for hormones, antibodies and other biological mediators, as well as many metabolic agents, including cancer promoters.

These negatively charged terminals appear to play a key role in the first detection of weak electrochemical oscillations in the pericellular fluid, including tissue components of environmental fields. They attract a cationic atmosphere, with Ca^{2+} and H^+ ions predominating at the protein binding sites.

3.b. Observed Sensitivities to Imposed Electromagnetic Fields

As a perspective on the biological significance of cell-surface current flow through narrow spaces between cells, there is evidence from a number of studies that ELF fields in the range 0-100 Hz and RF/microwave fields amplitude-modulated in this same ELF range, producing tissue gradients in the range 10^{-7}–10^{-1} V/cm, are involved in essential physiological functions in marine vertebrates, birds and mammals (see Adey, 1981, 1990, 1992, for reviews). *In vitro* studies have reported similar sensitivities for cerebral Ca^{2+} efflux, and in a wide spectrum of Ca^{2+}-dependent processes that involve cell membrane functions: bone growth, modulation of intercellular communication mechanisms that regulate cell growth, reduction of cell-mediated cytolytic immune responses, and modulation of intracellular enzymes that are molecular markers of signals arising at cell membranes and then coupled to the cell interior.

3.c. The Transductive Step: Possible Role of Free Radicals in Cell Detection of Low-Level Electromagnetic Fields

i). The thermal model: constraints on field thresholds in equilibrium thermodynamic models. If tissue heating determines threshold sensitivity, excitation requires interaction with energy greater than the average thermal (kT) energy.

A general physical statement forbids direct quantum steps as primary mechanisms in biomolecular systems for electromagnetic fields in the spectrum from DC to microwaves. Only above the infrared region is photon quantum energy sufficient for ionization or molecular dissociation. Below the mid-infrared region, (f = 6 THz), photon energy hf is smaller than kT = 1/40 eV. Since this is the average energy in any molecular degree of freedom, photon absorption cannot significantly increase, for example, a vibrational amplitude. Moreover, all molecular vibrational degrees of freedom are tightly coupled and relax in a few picoseconds. ***Thus, there would be no enhancement in mean energy by sequential absorption of photons*** (Grundler et al., 1992).

ii). The athermal model: possible role of free radicals in a non-equilibrium model. Mounting evidence confirms that bioeffects occur in environmental electromagnetic fields that are dwarfed by much larger intrinsic bioelectric processes, and may also be substantially below levels of tissue thermal noise. In the search for an understanding of the first transductive steps. A role has been proposed for chemically very reactive free radicals (for reviews, see Grundler et al., 1992; McLauchlan, 1992).

In chemical reactions, bonds break and reform. Most bonds consist of paired electrons with opposite spins, with one electron derived from each partner to in the union. When bonds break in a chemical reaction, each partner reclaims its electron from the bond and moves away to encounter a new partner. It is now an unattached *free radical*. Reforming a bond requires a meeting between two radicals with opposite electron spins, the union producing a ***singlet pair***. No union results from encounters between radicals with the same spins.

There are important emergent considerations in extrapolating this model to bioelectromagnetic sensitivities (Grundler et al., 1992). Although lifetimes of free radicals are short, typically in the range of nanoseconds to picoseconds, 1) they are extremely sensitive to static and oscillating magnetic fields; 2) McLauchlan points out that this sensitivity "***begins at the lowest applied field strength***"; 3) the effect is quite general and does not depend on any specific identity of the radicals; 4) electron spin energies are conserved through thermal collisions, and thus, ***thresholds for biological sensitivities may extend far below thermal collisional energies (kT) in tissue***; 5) in these interactions, "There is an enormous effect of a small magnetic field on a chemical reaction....The all-important interaction has an energy very much less than the thermal energy of the system, and is effective exclusively through its influence on the kinetics; this is counter-intuitive to most scientists" (McLauchlan, 1992).

3.d. Cell Membrane Amplification: Trans-membrane Signaling and Coupling to a Cascade of Intracellular Enzymes

Beyond the first transductive step, amplification is essential before weak electrical and chemical signals at cell membrane surfaces are coupled to the cell interior. Available evidence favors cooperative processes in the binding and release of Ca^{2+} at charge sites on surface protein strands, with response "windows" in frequency and amplitude (Adey, 1992). There may be a required minimum duration of exposure (***coherence time***) at a specific ELF modulation frequency before intracellular enzymes respond. Krause (1990) observed no responses with short coherence times (0.1-1.0 sec), but epochs of 10 and 50 sec enhanced enzyme activity.

Transmembrane signaling occurs along receptor protein strands. Much further research will be necessary to elucidate underlying physical processes, which have been modeled on the basis of dark soliton propagation (Adey, 1993), transmembrane electron tunneling (DeVault and Chance, 1966), and concurrent electron tunneling and nuclear vibrations (Hoth and Penner, 1992; Moser et al., 1992).

Within the cell, the amplified signal activates an enzyme cascade. ELF and ELF-modulated RF fields modulate major enzyme sequences that signal surface stimuli to the cell interior (Luben et al. 1982; 1991) and via messenger protein kinases (Byus te al., 1984) and the growth regulating enzyme ODC (Byus et al., 1988), to cell nuclei where they alter gene expression (Goodman and Henderson, 1988; Phillips et al., 1992).

4. Laboratory Studies Related to Regulation of Cell Growth

Mechanisms regulating cell growth may be classified in two broad categories. Both have been found sensitive to environmental electromagnetic fields.

Some controls are mediated through functions of major body systems; as through the immune system, which, in making the fundamental distinction between "self" and "not-self", targets malignant cells for destruction; or through brain hormone mechanisms, such as melatonin secretion by the pineal gland, where there is modulation of estrogen receptor formation in the breast, a known factor in certain types of breast cancer.

In a second category, regulation of cell growth appears to lie in local mechanisms at the cellular level. Control may be lost when there is disruption of intercellular communication through paths that depend on direct cell-cell contact.

4.a. Field Effects on Cell Growth Regulation by Immune Mechanisms

Cell studies have shown effects of both ELF and RF fields on immune mechanisms.

After stimulation of lymphocytes with a mitogen, calcium uptake into the cells is increased. This uptake is further enhanced by 60 Hz magnetic fields but decreased by 3 Hz fields (Walleczek, 1992). There was no field effect in the absence of the mitogen, again pointing to a field action that modulates an on-going chemical reaction. Allogeneic cytotoxicity, in which lymphocytes destroy a target of tumor cells by making physical contact with them, was reduced 20% in ELF-modulated 450 MHz fields in a modulation frequency-dependent manner (Lyle et al., 1983), and in 60 Hz electric fields by 38% (Lyle et al., 1988). In human lymphocytes, a 450 MHz field with 16 Hz sinusoidal modulation transiently decreased protein kinase enzyme activity by 60% in the first 20 min of exposure, but it was without continuing effect beyond 45 min (Byus et al., 1984).

4.b. Low-Level Electromagnetic Fields as Co-Promoters in Tumor Formation: Epigenetic Models of Carcinogenesis

Cell growth is commonly measured by an increase in cell numbers, or by an increase in the synthesis of DNA.

i) DNA synthesis in isothermal microwave exposures. In RF/microwave studies, DNA synthesis has been tested in blood lymphocytes and human brain tumor (glioma) cells exposed to high (thermalizing) field levels, yet maintained in isothermal conditions (Cleary et al., 1992). With 2.45 GHz CW fields and adsorbed energy (SARs) in the range 4 to 50 W/kg, lymphocyte DNA synthesis was increased at intermediate field levels, but was suppressed at the highest levels. Glioma cells responded with similar increases at SARs up to 50 W/kg, but synthesis decreased at 80 W/kg.

These studies indicate direct mechanisms of interaction that induce protracted functional alterations not attributable to indirect thermal effects. However, these exposures exceed by about two orders of magnitude fields induced in the head by currently accepted hand-held devices; nor does the experimental technique suggest extrapolation of these findings to unregulated cell growth that results in tumor formation.

ii) Frequency dependence of cell growth in millimeter wave fields. Collaborative studies of yeast cell growth over the past 15 years using athermal millimeter wave fields (Grundler and Keilmann, 1978; Grundler and Kaiser, 1992) have shown that growth appears finely "*tuned*" to applied frequencies around 42 GHz, with successive peaks and troughs at intervals of about 10 MHz. In recent studies, they noted that the sharpness of the tuning increased as the intensity of the imposed field decreased; but the tuning peak occurred at the same frequency when the field intensity was progressively reduced. Moreover, clear responses occurred with incident fields as weak as 5 picowatts/cm^2.

iii). Disruption of intercellular communication and tumor promotion: epigenetic carcinogenesis. Tumor formation as a manifestation of abnormal control of cell growth is now widely modeled as a multistep process, based on animal tumor models. *Epigenetic carcinogenesis* describes a sequence of initiation-promotion-progression in tumor formation. *Initiation* is a single event involving damage to DNA in the cell nucleus by action of mutagenic substances or agents such as ionizing radiation. Initiated or transformed cells may remain indefinitely in this condition without tumor formation. Tumor formation requires subsequent *promotion* by repeated intermittent exposure to agents which are not mutagenic, and thus are not cancer initiators by an action on DNA in the nucleus.

Promoters include pesticides and insecticides such as DDT, polychlorbiphenyls (PCBs) formerly used as electrical insulators and coolants, saccharin, and plant lectins now used as cancer promoters in laboratory studies, the phorbol esters. Promotion studies in cultured cells and animal models have examined joint actions of phorbol esters and electromagnetic fields, *since both act at cell membranes, and fields may act as co-promoters.*

Available evidence indicates that nonionizing electromagnetic fields do not act as classical initiators by causing DNA damage and gene mutation. There is considerable evidence for their promoting action at cell membranes, in concert with chemical agents (Adey, 1990b). Promotion may involve a distorted inward signal stream from cell membranes directed to the nucleus and other organelles (Adey, 1992b); and at the same time, there may be disruption of an outward signal stream essential for normal communication between cells (Yamasaki, 1991). ***Gap-junctions*** are small plaques of protein that make a passage for these intercellular signals.

iv). Experimental evidence on synergic actions of electromagnetic fields and chemical promoters in tumor promotion. Cells with well developed gap-junctions can prevent entry of toxic substances. Gap-junction communication is damaged by phorbol esters. This action is further enhanced by a 450 MHz, 1.0 mW/cm^2 field modulated at 16 Hz (Fletcher et al., 1986). Also, there is evidence for persistent cell membrane effects in embryonic fibroblast cells treated with phorbol esters after X-ray irradiation and prolonged (24 h) microwave exposure (Balcer-Kubiczek and Harrison, 1985).

More direct evidence on growth regulation comes from co-culture (in the same dish) of normal parent fibroblast cells together with their daughters mutated by ultraviolet light (Cain et al., 1993). The mutant cells showed unregulated growth, heaping up on themselves to form small foci, or "cancers in a dish"; but when grown together with their parents, physical contact between them and the parents inhibits their unregulated growth. This equilibrium is disrupted by minute doses of phorbol ester, with reappearance of tumor foci; addition of a 60 Hz 1 gauss field approximately doubled the number, size and cell density of foci. By contrast, no effects were found in this co-culture system from exposure to an 800 MHz field with TDMA modulation proposed for a new mobile communication system (Table 1).

A skin cancer model in mice, based on this same phorbol ester tumor promotion model following chemical initiation, has shown an initial increased tumor incidence with exposures to a 60 Hz 1 gauss field (Stuchly et al., 1991).

5. Bridges from Laboratory Research to Epidemiological Findings

What has been learned from laboratory studies that may be relevant to possible health hazards from environmental electromagnetic fields?

a. Disclosure of a variety of ON- and OFF-effects in cellular responses suggests that there may be a special significance to intermittent exposures. These effects have been noted in key enzyme responses, including those involved in regulation of cell growth. Their importance has been recognized in determining therapeutic regimes utilizing electromagnetic fields. They point to the need for further laboratory research in evaluating magnetic transients associated with domestic and industrial systems.

b. RF/microwave fields that are pulse- or amplitude-modulated at ELF frequencies may interact strongly with cells and tissues in ways not seen with unmodulated fields under the same exposure conditions.

c. Modulation frequency "windows" suggest a specificity for certain particular field characteristics in biomolecular interactions. They offer strong support for an athermal basis in many bioeffects observed with both ELF and modulated RF/microwave fields.

d. At the core of epidemiological studies is the question of cumulative dose. This is vastly more complex than for ionizing radiation, where the simple product of field intensity and exposure duration has long been the generally adopted criterion. Here, there is the recognized importance of intermittency, the complex spectral and temporal field characteristics of normal daily exposures, and possible concurrent actions of fields with a myriad chemical promoting factors, many unknown or unrecognized.

e. An emergent conclusion from laboratory studies is the likelihood that mechanisms of biomolecular interactions with nonionizing electromagnetic fields are multiple and hierarchical.

f. Laboratory studies have provided a first approach to mechanisms mediating health related field effects in 1) embryonic and fetal development; 2) modulation of immune functions; 3) regulation of cell growth and development, including cancer; and 4) interactions in the central nervous system, including brain hormone cycling.

g. The emergent field of bioelectromagnetics now offers a bridge between studies of the physics of matter and the search for essential bioenergetics of living systems, primarily through collaborative research at the cutting edges of each of these fields. These are developments towards a physical biology. To sustain this level of joint endeavor, and more importantly, to carry it forward in a broad vista of future research, mainstream biological science is coming to recognize the essential significance of athermal interactions based in nonequilibrium processes and long range atomic interactions.

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